UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,877	04/17/2002	Toshio Miyata	2605/102	5152

2101 7590 01/27/2005

BROMBERG & SUNSTEIN LLP
125 SUMMER STREET
BOSTON, MA 02110-1618

EXAMINER
HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 01/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,877	MIYATA, TOSHIO	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The following Office action is in response to Applicant's reply filed 11/1/04 wherein claims 1-14 and 16 were cancelled. New claim 17 was added. Claims 15 and 17 are presented for examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyata et al. (Feb. 1999, reference EL in the IDS) in view of Ulrich et al. (US 5,272,176), Ohuchida (EP 323,590) and Davankov et al. (1997).

Miyata et al. disclose that carbonyl stress in uremia may contribute to long-term complications associated with chronic renal failure and dialysis. Carbonyl compounds such as glyoxal are responsible for reacting with carbohydrates and lipids to form advanced glycation products (abstract). The level of the AGE pentosidine is markedly raised in uremic plasma. However, conventional hemodialysis and peritoneal dialysis do not significantly modify total pentosidine (p. 390, left column, end of 2nd paragraph). Miyata et al. disclose that aminoguanidine and OPB-9195 (2-isopropylidenehydrazono-4-oxo-thiazolidin-5-ylacetanilide) inhibit AGE formation by reacting with carbonyl compounds responsible for AGE-formation. Miyata et al. teach that AGE inhibitors can be administered orally or be immobilized in cartridges to extract reactive carbonyl compounds from blood during blood dialysis therapy, as in claims 3, 4 and 12 (p. 396, right column).

Miyata et al. do not teach that the reduction of a carbonyl stress state in blood can be accomplished with a sulfonylhydrazine group immobilized on a crosslinked polystyrene carrier.

Ulrich et al. disclose compounds for inhibiting the non-enzymatic crosslinking of proteins by reacting the early carbonyl glycosylation products that are responsible for the crosslinking. The agents comprise compounds of formula I wherein a benzene ring is substituted by a carbonyl group and one or two amino, hydrazine or hydrazinosulfonyl groups (col. 4, lines 40-68). The carbonyl-trapping agents can be administered orally.

Ohuchida discloses hydrazine derivatives that eliminate carbonyl compounds that cause excessive crosslinking of proteins. Ohuchida teaches that the terminal amino group of the hydrazine moiety is responsible for reacting with said carbonyl compound (Scheme on p. 4). The activity of the discloses hydrazine-bearing compounds is compared to guanidine which is known to inhibit the crosslinking of collagen (p. 5, lines 2-12).

Davankov et al. disclose that Styrosorb is a hypercrosslinked polystyrene that can serve as a sorbent for blood impurities in dialysis (p. 120, left column, 2nd paragraph). Styrosorb can be chemically modified to selectively absorb certain types of molecules from the blood. For example, by a chain of trivial reaction, a lipid-pike layer can be synthesized on the surface of the cross-linked polymer. The modified surface is capable of absorbing free phospholipids from blood (p. 121, left column, 2nd paragraph).

It would have been obvious to one of ordinary skill in the art to improve the carbonyl stress state in a person's blood by hemodialysis with a carbonyl-trapping compound comprising a crosslinked polystyrene bound to a sulfonyl hydrazine. The ordinary artisan would have been motivated to do so because the trapping groups, guanidine and sulfonylhydrazine, are known to work by the same mechanism for the same purpose. Thus, the ordinary artisan would have expected a reasonable expectation of success that a sulfonylhydrazine groups could be substituted for a guanidine group on a carrier because non-immobilized guanidinium- and sulfonylhydrazine-containing compounds are employed as orally administered carbonyl-trapping agents. It is known that guanidinium compounds can be immobilized on supports for trapping carbonyl compounds in blood dialysis. Thus, in the absence of

evidence to the contrary, guanidine and sulfonylhydrazine groups are interchangeable for the trapping carbonyl compounds in blood. The ordinary artisan would have been motivated to employ a crosslinked polystyrene carrier because said carriers are standard in the art for use as hemodialysis sorbents, as disclosed by Davánkov et al. The ordinary artisan could reasonably expect that a sulfonylhydrazine group could be coupled to crosslinked polystyrene because Davankov et al. disclose that such chemical modifications are well known in the art and Ulrich teaches compounds having the desired structure wherein a hydrazine group is bonded to a sulfonyl group that in turn is bonded to a benzene ring.

Double Patenting

Claims 15 and 17 are provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 27, 29 and 34-36 of copending Application No. 09/763,286, in view of Miyata et al. (Feb. 1999, reference EL in the IDS) in view of Ulrich et al. (US 5,272,176), Ohuchida (EP 323,590), Davankov et al. (1997), Elahi (US 4,131,544) and Ash (EP 064,393).

'286, is directed a method preparing a peritoneal dialysate having a reduced carbonyl stress state, wherein blood is passed through a cartridge that is capable of removing carbonyl compounds. Claims 20, 21, 27, 29 and 37 represent the genus of carbonyl trapping agents. Dependent claims 34 and 36 of '286 recite that the cartridge is composed of a hydrazine derivative. The sulfonyl hydrazine group of the instant claims is a specie of carbonyl trapping agents that is a member of the genus of carbonyl trapping agents of '286. Claim 35 of '286 is directed to a sulfonylhydrazine derivative which is the carbonyl trapping agent specie recited in instant claims 15 and 17. The remaining claims are drawn to guanidinium-derived carbonyl trapping agents.

'286 does not teach that the removal of carbonyl compounds from a peritoneal dialysate can be employed for removing carbonyl compounds via a hemodialysis in a circuit, that the cartridge comprises sulfonylhydrazine derivatives which are bound to cross-linked polystyrene or that sulfonylhydrazine moieties can provide the same carbonyl trapping ability as a guanidine-type trapping group.

The disclosure by Miyata et al. , Ulrich et al., Ohuchida and Davankov et al. are discussed *supra.*

Ash discloses a sorbent suspension reciprocating dialyzer comprising a surface adsorptive agent capable of adsorbing uremic substances, a cation exchanger, urease, an aliphatic carboxylic acid resin, water and a suspending agent (abstract). Ash teaches that the sorbet mixture is equally useful in hollow filter dialyzers (hemodialysis) or in a peritoneal dialysis unit with a suitable dialyzer to cycle the peritoneal dialysate into and out of the abdomen (p. 13-14, bridging).

Elahi teaches encapsulated sorbent element that is confined within a rigid porous filter membrane that is suitable for adsorbing matter from liquid media. The sorbent can be used in hemodialysis, hemoperfusion and peritoneal dialysis (abstract and col. 12, lies 30-40).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the trapping of carbonyl species in the peritoneal fluid that is claimed in '286 to a method of trapping carbonyl species via hemodialysis with sulfonylhydrazine derivatives bound to a crosslinked polystyrene. The ordinary artisan would have been motivated to apply a method that removes carbonyl compounds from a peritoneal dialysate with a cartridge that traps said carbonyl compounds (the method of '286) to a hemodialysis circuit because Elahi and Ash demonstrate that a sorbent that is used to remove toxins from biological fluids for peritoneal dialysis can also be applied to hemodialysis for the same purpose. The ordinary artisan would have had a reasonable expectation that a sorbent for removing toxins from a biological fluid would be suitable for both peritoneal dialysis and hemodialysis because Ash and Elahi clearly disclose that a sorbent can be used for either method since said methods serve the same purpose (removal of toxins).

The ordinary artisan would be motivated to employ a cartridge comprising crosslinked polystyrene that is conjugated to a carbonyl trapping agent because it cross-linked polystyrene is recognized as a desirable adsorbent for hemodialysis and that its efficiency can be increased by chemically modifying it with suitable biologically active compounds. The ordinary artisan would have had a reasonable expectation that crosslinked polystyrene could be derivatized to serve as an adsorbent

for hemodialysis because Davankov et al. disclose methods and examples for chemical modification that are standard in the art.

The ordinary artisan would have been motivated to employ a sulfonylhydrazine group on a cartridge bearing guanidine trapping groups because guanidine and sulfonylhydrazine groups are both known to trap harmful carbonyl species in biological fluids. Thus, the ordinary artisan would have had had a reasonable expectation of success that a sulfonylhydrazine groups could be substituted for a guanidine group on a carrier because non-immobilized guanidinium- and sulfonylhydrazine-containing compounds are employed as orally administered carbonyl-trapping agents. It is known that guanidinium compounds can be immobilized on supports for trapping carbonyl compounds in blood dialysis. Thus, in the absence of evidence to the contrary, guanidine and sulfonylhydrazine groups are interchangeable for the trapping carbonyl compounds in blood.

This is a provisional obviousness-type double patenting rejection.

Claims 15 and 17 are provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 15, 22-30 and 32-36 of copending Application No. 10/089,789, in view of Miyata et al. (Feb. 1999, reference EL in the IDS) in view of Ulrich et al. (US 5,272,176), Ohuchida (EP 323,590), Davankov et al. (1997) and Beisswenger et al. (Jan. 1999).

'789 is drawn to a method of removing carbonyl compounds comprising contacting a carrier having immobilized biguanide with a body fluid such as blood, blood plasma, or a peritoneal dialysate via blood filtration, dialysis, blood adsorption or blood plasma separation.

'789 does not teach that the carbonyl trapping agent compounds comprises sulfonylhydrazine derivatives which are bound to cross-linked polystyrene and that said carbonyl strapping is executed via a hemodialysis circuit.

The disclosure by Miyata et al. , Ulrich et al., Ohuchida and Davankov et al. are discussed *supra.*

Beisswenger et al. disclose that the administration of metformin, a biguanide, to Type 2 diabetics reduced systemic levels of an α-dicarbonyl, methylglyoxal, which is a precursor for advanced glycation end products (abstract).

It would have been obvious to one of ordinary skill in the art to improve the carbonyl stress state in a person's blood by a hemodialysis circuit with a carbonyl-trapping compound comprising a crosslinked polystyrene bound to a sulfonylhydrazine. The ordinary artisan would have been motivated to do so because the trapping groups, guanidine, biguanide and sulfonylhydrazine, are known to work by the same mechanism for the same purpose. Thus, the ordinary artisan would have expected a reasonable expectation of success that a sulfonylhydrazine groups could be substituted for a biguanide group on a carrier because non-immobilized guanidine, biguanide- and sulfonylhydrazine-containing compounds are employed as orally administered carbonyl-trapping agents. It is known that guanidinium and biguanide compounds can be immobilized on supports for trapping carbonyl compounds in blood dialysis. Thus, in the absence of evidence to the contrary, guanidine, biguanide and sulfonylhydrazine groups are interchangeable for the trapping carbonyl compounds in blood. The ordinary artisan would have been motivated to employ a crosslinked polystyrene carrier because said carriers are standard in the art for use as hemodialysis sorbents, as disclosed by Davankov et al. The ordinary artisan could reasonably expect that a sulfonylhydrazine group could be coupled to crosslinked polystyrene because Davankov et al. disclose that such chemical modifications are well known in the art and Ulrich teaches compounds having the desired structure wherein a hydrazine group is bonded to a sulfonyl group that in turn is bonded to a benzene ring.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
AU 1651

JEAN C. WITZ
PRIMARY EXAMINER